(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 November 2000 (30.11.2000)

PCT

(10) International Publication Number
WO 00/71715 A1

(51) International Patent Classification[7]: C12N 15/16, 15/18, 15/63, 1/21, 5/00, G01N 33/53, A61K 38/18, C07K 14/50, 16/22

(21) International Application Number: PCT/US00/13331

(22) International Filing Date: 16 May 2000 (16.05.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/135,524 21 May 1999 (21.05.1999) US

(71) Applicant *(for all designated States except US)*: **HUMAN GENOME SCIENCES, INC.** [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **ROSEN, Craig, A.** [US/US]; 22400 Rolling Hill Road, Laytonville, MD 20882 (US). **ALDERSON, Ralph** [US/US]; 12125 Orchard View Road, Gaithersburg, MD 20878 (US). **MELDER, Robert** [US/US]; 14407 Saturn Way, Boyds, MD 20841 (US). **DUAN, Roxanne, D.** [US/US]; 5515 Northfield Road, Bethesda, MD 20817 (US). **HU, Jing-Shan** [CN/US]; 1247 Lake Side Drive, No. 3034, Sunnyvale, CA 94086 (US).

(74) Agents: **WALES, Michele, M.** et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).

(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/71715 A1

(54) Title: FIBROBLAST GROWTH FACTOR 11

(57) Abstract: The present invention relates to a novel human protein called Fibroblast Growth Factor 11, and isolated polynucleotides encoding this protein. Also provided are vectors, host cells, antibodies, and recombinant methods for producing this human protein. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to this novel human protein.

Fibroblast Growth Factor 11

Field of the Invention

The present invention relates to a novel human gene encoding a polypeptide which is a member of the Fibroblast Growth Factor family. More specifically, the present invention relates to a polynucleotide encoding a novel human polypeptide named Fibroblast Growth Factor 11, or "FGF-11." This invention also relates to FGF-11 polypeptides, as well as vectors, host cells, antibodies directed to FGF-11 polypeptides, and the recombinant methods for producing the same. Also provided are diagnostic methods for detecting and treating disorders. The invention further relates to screening methods for identifying agonists and antagonists of FGF-11 activity.

Background of the Invention

Fibroblast growth factors are a family of proteins characteristic of binding to heparin and are, therefore, also called heparin binding growth factors (HBGF). Expression of different members of these proteins are found in various tissues and are under particular temporal and spatial control. These proteins are potent mitogens for a variety of cells of mesodermal, ectodermal, and endodermal origin, including fibroblasts, corneal and vascular endothelial cells, granulocytes, adrenal cortical cells, chondrocytes, myoblasts, vascular smooth muscle cells, lens epithelial cells, melanocytes, keratinocytes, oligodendrocytes, astrocytes, osteoblasts, and hematopoietic cells.

Each member has functions overlapping with others and also has its unique spectrum of functions. In addition to the ability to stimulate proliferation of vascular endothelial cells, both FGF-1 and 2 are chemotactic for endothelial cells and FGF-2 has been shown to enable endothelial cells to penetrate the basement membrane. Consistent with these properties, both FGF-1 and 2 have the capacity to stimulate angiogenesis. Another important feature of these growth factors is their ability to promote wound healing. Many other members of the FGF family share similar activities with FGF-1 and 2 such as promoting angiogenesis and wound healing. Several members of the FGF family have been shown to induce mesoderm formation and to modulate differentiation of neuronal cells, adipocytes and skeletal muscle cells.

Other than these biological activities in normal tissues, FGF proteins have been implicated in promoting tumorigenesis in carcinomas and sarcomas by promoting tumor vascularization and as transforming proteins when their expression is deregulated.

```
Glu Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr
            100                 105                 110

Ile Ser Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys
        115                 120                 125

Asn Gly Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala
    130                 135                 140

Ile Leu Phe Leu Pro Leu Pro Val Ser Ser Asp
145                 150                 155


<210> 8
<211> 210
<212> PRT
<213> Homo sapiens

<400> 8
Leu Gly Asp Arg Gly Arg Gly Arg Ala Leu Pro Gly Gly Arg Leu Gly
  1               5                  10                  15

Gly Arg Gly Arg Gly Arg Ala Pro Glu Arg Val Gly Gly Arg Gly Arg
             20                  25                  30

Gly Arg Gly Thr Ala Ala Pro Arg Ala Ala Pro Ala Ala Arg Gly Ser
         35                  40                  45

Arg Pro Gly Pro Ala Gly Thr Met Ala Ala Gly Ser Ile Thr Thr Leu
     50                  55                  60

Pro Ala Leu Pro Glu Asp Gly Gly Ser Gly Ala Phe Pro Pro Gly His
 65                  70                  75                  80

Phe Lys Asp Pro Lys Arg Leu Tyr Cys Lys Asn Gly Gly Phe Phe Leu
                 85                  90                  95

Arg Ile His Pro Asp Gly Arg Val Asp Gly Val Arg Glu Lys Ser Asp
             100                 105                 110

Pro His Ile Lys Leu Gln Leu Gln Ala Glu Glu Arg Gly Val Val Ser
         115                 120                 125

Ile Lys Gly Val Cys Ala Asn Arg Tyr Leu Ala Met Lys Glu Asp Gly
     130                 135                 140

Arg Leu Leu Ala Ser Lys Cys Val Thr Asp Glu Cys Phe Phe Phe Glu
145                 150                 155                 160

Arg Leu Glu Ser Asn Asn Tyr Asn Thr Tyr Arg Ser Arg Lys Tyr Thr
                165                 170                 175

Ser Trp Tyr Val Ala Leu Lys Arg Thr Gly Gln Tyr Lys Leu Gly Ser
            180                 185                 190

Lys Thr Gly Pro Gly Gln Lys Ala Ile Leu Phe Leu Pro Met Ser Ala
        195                 200                 205
```

Lys Ser
210

<210> 9
<211> 111
<212> PRT
<213> Homo sapiens

<400> 9
Met Ser Gly Pro Gly Thr Ala Ala Val Ala Leu Leu Pro Ala Val Leu
1 5 10 15

Leu Ala Leu Leu Ala Pro Trp Ala Gly Arg Gly Gly Ala Ala Gly Ile
20 25 30

Lys Arg Leu Arg Arg Leu Tyr Cys Asn Val Gly Ile Gly Phe His Leu
35 40 45

Gln Ala Leu Pro Asp Gly Arg Ile Gly Gly Ala His Ala Asp Thr Arg
50 55 60

Asp Ser Leu Leu Glu Leu Ser Pro Val Glu Arg Gly Val Val Ser Pro
65 70 75 80

Gly Met Phe Ile Ala Leu Ser Lys Asn Gly Lys Thr Lys Lys Gly Asn
85 90 95

Arg Val Ser Pro Thr Met Lys Val Thr His Phe Leu Pro Arg Leu
100 105 110

<210> 10
<211> 208
<212> PRT
<213> Homo sapiens

<400> 10
Met Ala Leu Gly Gln Lys Leu Phe Ile Thr Met Ser Arg Gly Ala Gly
1 5 10 15

Arg Leu Gln Gly Thr Leu Trp Ala Leu Val Phe Leu Gly Ile Leu Val
20 25 30

Gly Met Val Val Pro Ser Pro Ala Gly Thr Arg Ala Asn Asn Thr Leu
35 40 45

Leu Asp Ser Arg Gly Trp Gly Thr Leu Leu Ser Arg Ser Arg Ala Gly
50 55 60

Leu Ala Gly Glu Ile Ala Gly Val Asn Trp Glu Ser Gly Tyr Leu Val
65 70 75 80

Gly Ile Lys Arg Gln Arg Arg Leu Tyr Cys Asn Val Gly Ile Gly Phe
85 90 95

His Leu Gln Val Leu Pro Asp Gly Arg Ile Ser Gly Thr His Glu Glu
100 105 110